REMARKS

Claims 42-93 are active in this application.

Support for the stringent hybridization conditions is found at least at page 5, lines 4-11. Support for Claims 74-93 are found in Claims 42-73 and the specification as originally filed. The specification has been amended to correct the date of the PCT application to which this application claims priority. A substitute Sequence Listing is provided herewith and includes SEQ ID NO:8, which was the original SEQ ID NO:3. The specification has been amended at page 15 to insert a sequence identifier (SEQ ID NO:) for this sequence. In addition, a computer-readable Sequence Listing corresponding to the paper copy is also submitted herewith. The contents of the paper copy and the computer readable sequence listing are identical. No new matter is added.

Applicants wish to thank the Examiner for withdrawing several objections and rejections as noted on page 3 of the Official Action. In light of the amendments and remarks submitted herein, Applicants respectfully request that all rejections be withdrawn and the present application be passed on to issuance.

The rejection of Claims 42-73 under 35 U.S.C. §112, first paragraph (written description) is respectfully traversed.

The terms "portion" and "fragment" are no longer present in the present claims. The claims as amended herein include a purified nucleic acid comprising SEQ ID NO:3 or SEQ ID NO:4. These sequences are unquestionably described in the application (see the Sequence Listing). The claims also include a sequence hybridizing with a complementary strand of SEQ ID NO:3 or SEQ ID NO:4 under specified conditions and which have either transcriptional promoter activity (e.g., see Claim 42) or encode a peptide that functions as a signal peptide (e.g., see Claim 60). Provided with the nucleotide sequences of SEQ ID NO:3

and 4, the tools generally available to hybridize one DNA to another DNA, and the knowledge of transcriptional promoter activity and signal secretion activity as described in the specification, the claims are deemed to be adequately described. In addition, Applicants respectfully direct the Examiner's attention to the U.S. PTO "Synopsis of Application of Written Description Guidelines" and, in particular, Example 9 (a copy is attached for reference).

In this example a situation that is analogous to the issue in the present claims is presented. The conclusion is that the claim in the Example, which is similar to the present claims in terms of providing for a sequence which hybridizes under stringent conditions to an allowable DNA, is adequately described. Therefore, the present claims are described because "a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that Applicant was in possession of the claimed invention." (see Example 9 of the "Synopsis").

The terms "toxin" and "variant" have also been removed from the present claims. In light of the above, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph.

Similarly, since the terms "proportion," "fragment," and "variant" have been removed from the claims the rejection under 35 U.S.C. §112, second paragraph is obviated by amendment.

The rejection of Claims 56-57, 59, 61, 71-73 under 35 U.S.C. §112, first paragraph (enablement) is respectfully traversed for the following reasons.

The Examiner has taken the position that the specification only enables the transformation expression of a prokaryotic host cell with a coding sequence for a *Clostridium*

perfringens beta toxin 1, which are controlled by SEQ ID NO:3 and a signal sequence encoded by SEQ ID NO:4 (referring to the discussion on pages 7-8 of the Official Action). Applicants disagree.

As known in the art at the time of filing, prokaryotic signal peptides can direct the secretion of proteins in mammalian cells (as discussed in the attached publication of Hall et al (1990), The Journal of Biological Chemistry, Vol. 265 (32), pp. 19996-19999). In addition, the Applicants have described that the vectors in this application, which have the transcriptional promoter or the signal secretion encoding sequence can be used to express any DNA of interest—referring to the specification on page 20, lines 17-23. This statement is also confirmed by Perez-Rueda et al (J. Mol. Biol. (1998) 275, pp. 165-170). In this publication, Perez-Rueda et al describe common features of transcriptional domains in both prokaryotic and eukaryotic systems: " Strongly preferred positions of activator binding sites occur in both *Escherichia coli* and eukaryotes, suggesting specific common features of transcription in the two systems" (see the Abstract). For example, on page 166, col. 2, last paragraph, Perez-Rueda et al describe the "Another strong similarity in the two systems (Figure 1) is the remarkably small number of activation sites downstream of -35." Taken together, the knowledge in the art supports for common mechanisms of transcription thereby supporting the Applicants' disclosure on page 20.

As a result, one of skill in the art can certainly make and/or use the invention according to the full scope of Claim s56-57, 59, 61, 71-73 to express proteins in both prokaryotic and eukaryotic cells with the nucleic acid sequences provided in those claims. Withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 42, 45, 48-49, 50, 54-56, 61-65, 66-69, 71-73 under 35 U.S.C. §102(b) over Hunter et al is respectfully traversed.

Hunter et al does not describe SEQ ID NO:3 or SEQ ID NO:4. Furthermore, Hunter et al does not describe sequences which hybridize under stringent conditions to SEQ ID NO:3 or SEQ ID NO:4 such that those sequences have promoter activity or encode a peptide with signal secretion activity (see Claims 42 and 60). In fact, on page 3960, col. 2, third paragraph, Hunter et al describe that "the region between the putative ribosome binding site and the ATG start codon was composed entirely of thymidine residues. No potential promoter sequences were identified because of the high A+ T content of the DNA upstream of *cpb*."

Therefore, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is now in a condition for allowance. Early notification of such allowance is kindly requested.

Respectfully submitted,

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